

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
21 June 2001 (21.06.2001)

PCT

(10) International Publication Number
WO 01/43733 A3

(51) International Patent Classification⁷: **A61K 31/00**,
31/167, 31/245, 31/445, A61P 25/00, 25/06

(21) International Application Number: **PCT/US00/33916**

(22) International Filing Date:
15 December 2000 (15.12.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/170,817 15 December 1999 (15.12.1999) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
10 May 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/43733 A3

(54) Title: **COMPOSITIONS, KITS, APPARATUS, AND METHODS FOR INHIBITING CEPHALIC INFLAMMATION**

(57) Abstract: Methods, kits, apparatus, and compositions for inhibiting cephalic inflammation, including meningeal inflammation and cerebral inflammation for example, in a human patient are provided. The methods comprise intranasally administering to the patient a pharmaceutical composition comprising a local anesthetic, and preferably a long-acting local anesthetic ingredient. A composition useful for practising the methods of the invention is described which comprises at least one local anesthetic in a pharmaceutically acceptable carrier, wherein the composition is formulated for intranasal delivery. A kit comprising the composition and an intranasal applicator is also included in the invention. Apparatus for delivering or applying the compositions of the invention or for performing the methods of the invention are also described.

INTERNATIONAL SEARCH REPORT

I. International Application No

PCT/US 00/33916

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/00 A61K31/167 A61K31/245 A61K31/445 A61P25/00
A61P25/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, MEDLINE, BIOSIS, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 00 44432 A (LEVIN BRUCE H) 3 August 2000 (2000-08-03) the whole document ---	1-31
X	WO 99 03473 A (LEVIN BRUCE H) 28 January 1999 (1999-01-28) the whole document ---	1-31
X	WO 99 32103 A (ASTRA AB ;EEK ARNE (SE); DALSGAARD CARL JOHAN (SE); WALDENLIND LEN) 1 July 1999 (1999-07-01) the whole document ---	1-12, 19-23, 25-28,30
X	WO 98 38998 A (DARWIN DISCOVERY LTD) 11 September 1998 (1998-09-11) the whole document ---	1-8, 10-23, 25-28,30
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
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- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

9 November 2001

Date of mailing of the international search report

27/11/2001

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/33916

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 315 673 A (MERCK & CO INC) 11 February 1998 (1998-02-11) the whole document ---	1-8, 10-28, 30
X	BE 1 009 851 A (THIEBAULD CHARLES MARIE) 7 October 1997 (1997-10-07) the whole document ---	25-28, 30
X	EP 0 754 453 A (LIEDTKE PHARMED GMBH) 22 January 1997 (1997-01-22) the whole document ---	25-28, 30
X	C.A. CAPUTI ET AL.: "Therapeutic Blockage of Greater Occipital and Supraorbital Nerves in Migraine Patients" HEADACHE, vol. 37, no. 3, 1997, pages 174-179, XP001036584 the whole document ---	25-28, 30
A	PAPPAGALLO, MARCO (1) ET AL: "Imaging neurogenic inflammation in patients with migraine headaches." NEUROLOGY, (APRIL 12, 1999) VOL. 52, NO. 6 SUPPL. 2, PP. A274-A275. MEETING INFO.: 51ST ANNUAL MEETING OF THE AMERICAN ACADEMY OF NEUROLOGY TORONTO, ONTARIO, CANADA APRIL 17-24, 1999 AMERICAN ACADEMY OF NEUROLOGY. , XP001036585 cited in the application the whole document ---	1-31
A	"THE MERCK MANUAL" 1999, MERCK RESEARCH LABORATORIES XP002181662 page 1376 -page 1377 ---	1-31
A	MAIZELS M ET AL: "Intranasal lidocaine for treatment of migraine: a randomized, double-blind, controlled trial 'see comments!'" JAMA THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, CHICAGO, IL, US, vol. 276, no. 4, 24 July 1996 (1996-07-24), pages 319-321, XP002086201 ISSN: 0098-7484 the whole document ---	1-31

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/33916

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KUDROW L ET AL: "Rapid and sustained relief of migraine attacks with intranasal lidocaine: preliminary findings" HEADACHE, AMERICAN ASSOCIATION FOR THE STUDY OF HEADACHE,, US, vol. 35, no. 2, 1 February 1995 (1995-02-01), pages 79-82, XP002086202 ISSN: 0017-8748 the whole document -----</p>	1-31

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-10,12,17-31 relate to a compound defined by reference to a desirable characteristic or property, namely "long-acting local anesthetic".

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to its pharmacological profile. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Furthermore, present claims 11,18,24 relate to an extremely large number of possible compounds. Again support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds structurally identified in claims 13-16, with due regard to the general idea underlying the present invention.

Claims searched completely: 13-16

Claims searched incompletely: 1-12,17-31

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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